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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/931,457	02/22/2002	Saverio Carl Falco	BB1116 US CIP	3268

23906 7590 07/14/2004

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WILMINGTON, DE 19805

EXAMINER

BAUM, STUART F

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/931,457

Applicant(s)

FALCO ET AL.

Examiner

Stuart F. Baum

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 May 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16-26 is/are pending in the application.
- 4a) Of the above claim(s) 26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 16-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 2/22/2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2/15/02.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Art Unit: 1638

DETAILED ACTION

1. Applicant's election without traverse of Group I, claims 1-10, and 13-14 in the reply filed on 5/6/2004 is acknowledged.

Claims 16-26 are pending.

Claims 1-15 have been canceled.

Claims 16-26 have been newly added.

Newly submitted claim 26 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The claim does not correspond to either the originally presented claim 14 as asserted in Applicants' response (page 5, 4th paragraph), nor does it correspond to the instantly elected group.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 26 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. Claims 16-25 are examined in the present office action.

Inventorship

3. In view of the papers filed 5/6/2004, the inventorship in this nonprovisional application has been changed by the deletion of Stephen M. Allen.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Art Unit: 1638

Specification

4. The Specification is objected to because the drawings are not referred to properly. If the drawings show Figures 2A, 2B, and 2C, then the Brief Description of the Drawings should recite "Figures 2A-2C", instead of "Figure 2". Correction is requested.

Written Description

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 16-17 and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated polynucleotide encoding a polypeptide having cysteine gamma synthase activity wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity compared to SEQ ID NO:31, vector, recombinant DNA construct, cell, plant, seed and method of transforming a cell comprising said polynucleotide.

Applicants isolated a cDNA clone from soybean whose nucleic acid sequence is set forth in SEQ ID NO:30 encoding a cysteine gamma synthase of SEQ ID NO:31.

The Applicants do not identify essential regions of cysteine gamma synthase encoded by SEQ ID NO:30, nor do Applicants describe any polynucleotide sequences

Art Unit: 1638

that encode a polypeptide having at least 90% or 95% sequence identity to SEQ ID NO:31 that encodes a functional cysteine gamma synthase. The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In summary, the court stated that a written description of an invention requires a precise definition, one that defines the structural features of the chemical genus that distinguishes it from other chemical structures. A definition by function does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. The court goes on to say, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." *See University of California v. Eli Lilly and Co.*, 119 F.3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Applicants fail to describe a representative number of polynucleotide sequences encoding a cysteine gamma synthase falling within the scope of the claimed genus of polynucleotide sequences that encode a polypeptide having at least 90% or 95% sequence identity to SEQ ID NO:31. Applicants only describe a single cDNA sequence of SEQ ID NO:30. Furthermore, Applicants fail to describe structural features common to members of the claimed genus of polynucleotides. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for the cysteine gamma synthase, it remains unclear what features identify a cysteine gamma synthase. Since the genus of cysteine gamma

Art Unit: 1638

synthase has not been described by specific structural features, the specification fails to provide an adequate written description to support the breath of the claims.

Enablement

6. Claims 16-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The claims are drawn to an isolated polynucleotide encoding a polypeptide having cysteine gamma synthase activity wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity compared to SEQ ID NO:31, vector, recombinant DNA construct, cell, plant, seed and method of transforming a cell comprising said polynucleotide.

Applicants isolated a cDNA clone (Se3.05h06) from a soybean cDNA library made from young, 8-9 mm long fruits, the nucleic acid sequence of which is set forth in

Art Unit: 1638

SEQ ID NO:30 encoding a cysteine gamma synthase of SEQ ID NO:31 (page 25-28, Examples 1-2; page 34-36, Example 6).

Applicants do not reduce to practice their invention. Applicants do not teach by way of disclosure or example how one skilled in the art can use the isolated nucleic acid encoding a cysteine gamma synthase to increase the cysteine content in a corn or soybean plant (as purported in the paragraph bridging pages 1 and 2).

Wirtz et al (2003, Amino Acids (Vienna) 24 (1-2):195-203) teach that cysteine biosynthesis is a two-step process in plants and that serine acetyltransferase (SAT) is the rate limiting enzyme that catalyzes the first step of cysteine biosynthesis in conjunction with cysteine synthase (O-acetylserine (thiol) lyase) (page 195, 1st paragraph of 'Introduction'). Wirtz et al report that SAT is highly sensitive to feedback inhibition by cysteine (*ibid*). Therefore, transforming a plant with a nucleic acid encoding a cysteine synthase will not overcome the feedback inhibition of SAT, and hence, will not produce an increased concentration of the amino acid cysteine. The Office interprets cysteine gamma synthase, cysteine synthase, and O-acetylserine (thiol) lyase to have the same enzymatic activity as evidenced by Applicants disclosure (page 31, Table 14, NCBI GI numbers: GI 540497, GI 416869 and GI 11131628 all encode a cysteine synthase).

The state-of-the-art is such that one of skill in the art cannot predict which nucleic acids encoding a polypeptide that exhibits 90% or 95% sequence identity to SEQ ID NO:31 will encode a protein with the same activity as a protein encoded by SEQ ID NO:30. The prediction of protein structure from sequence data and, in turn, utilizing predicted structural determinations to ascertain functional aspects of the protein, is extremely complex, and the positions within the protein's sequence where amino acid

Art Unit: 1638

substitutions can be made with a reasonable expectation of maintaining function are limited (Bowie et al, Science 247:1306-1310, 1990, see especially page 1306). Proteins may be sensitive to alterations in even a single amino acid in a sequence. For example, the replacement of a glycine residue located within the START domain of either the PHABULOSA or PHAVOLUTA protein receptor with either an alanine or aspartic acid residue, alters the sterol/lipid binding domain (McConnell et al, Nature 411 (6838):709-713, 2001, see especially page 710, left column, 2nd paragraph).

Applicants have not disclosed how one makes or isolates any of the sequences that are encompassed by Applicants' broad claims. Applicants have not taught which regions of the respective polynucleotides can be used to amplify any of said polynucleotides or which regions can be used as a probe to isolate any of said polynucleotide sequences.

In the absence of guidance, undue trial and error experimentation would be required for one of ordinary skill in the art to screen through the multitude of non-exemplified sequences, either by using non-disclosed fragments of SEQ ID NO:30 as probes or by designing primers to undisclosed regions of SEQ ID NO:31 and isolating or amplifying fragments, subcloning the fragments, producing expression vectors and transforming plants therewith, in order to identify those, if any, that when over-expressed encode a polypeptide having cysteine synthase activity and exhibit 90% or 95% sequence identity with SEQ ID NO:31. In addition, undue trial and error experimentation would be required for one of skill in the art to identify and isolate a nucleic acid encoding a cysteine synthase and then transform a plant with said sequence for the purpose of

Art Unit: 1638

increasing the level of cysteine in the plant, given that cysteine synthase is not the rate limiting enzyme of cysteine biosynthesis.

Therefore, given the breadth of the claims; the lack of guidance and examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to practice the claimed invention, and therefore the invention is not enabled.

7. Claims 16-25 are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest an isolated polynucleotide of SEQ ID NO:30 encoding SEQ ID NO:31 and method for transforming a cell comprising said polynucleotide.

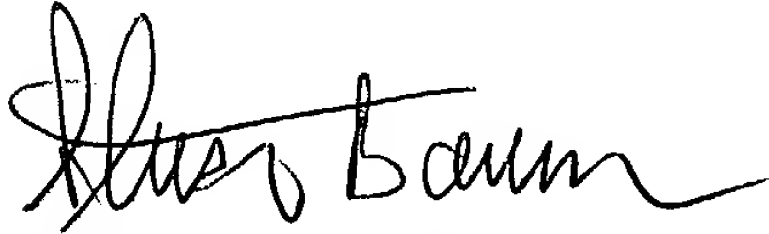
8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stuart F. Baum whose telephone number is 571-272-0792. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Art Unit: 1638

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

A handwritten signature in black ink, appearing to read "Stuart F. Baum". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

Stuart F. Baum Ph.D.

Patent Examiner

Art Unit 1638

July 9, 2004